

# WEST Search History

DATE: Tuesday, March 19, 2002

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
		result set	
side by side			
	<i>DB=JPAB,EPAB,DWPI; PLUR=NO; OP=ADJ</i>		
L14	L13 with (neutrali\$4 or inhibit\$3 or modulat\$3)	31	L14
L13	L12 near2 (antibod\$3 or immunoglobulin\$1)	143	L13
L12	(TNF or TNFa or aTNF or cachetin or ((tumor or tumour) adj necrosis adj factor))	3287	L12
	<i>DB=USPT; PLUR=NO; OP=ADJ</i>		
L11	L10 or l9	27	L11
L10	L8 and @prad<19910318	19	L10
L9	L8 and @ad<19910318	13	L9
L8	L7 with (neutrali\$4 or inhibit\$3 or modulat\$3)	182	L8
L7	L6 near2 (antibod\$3 or immunoglobulin\$1)	529	L7
L6	(TNF or TNFa or aTNF or cachetin or ((tumor or tumour) adj necrosis adj factor))	6249	L6
L5	L4 or l3	10	L5
L4	L2 and @prad<19910318	7	L4
L3	L2 and @ad<19910318	9	L3
L2	L1 and (TNF or TNFa or aTNF or cachetin or ((tumor or tumour) adj necrosis adj factor))	81	L2
L1	(antibod\$3 or immunoglobulin\$1) with (A2 or (A-2))	330	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 20:19:53 ON 19 MAR 2002)

FILE 'MEDLINE, BIOSIS, CANCERLIT, LIFESCI, BIOTECHDS' ENTERED AT  
20:20:18

ON 19 MAR 2002

L1 189290 S CACHETIN OR TNF OR TNFALPHA OR TNFA OR ((TUMOR OR  
TUMOUR) (W)N  
L2 5918 S L1 AND (A2 OR (A-2) OR MABA2 OR CA2 OR (MABA-2) OR (CA-2))  
L3 570 S L2 AND PY<1992  
L4 3164 S L1 AND (A2 OR (A-2))  
L5 413 S L4 AND PY<1992  
L6 183 DUP REM L5 (230 DUPLICATES REMOVED)  
L7 464333 S A2 OR (A-2) OR CA2 OR (CA-2) OR (C-A2) OR (C-A-2)  
L8 4285 S L7(S)L1  
L9 755 S L8(S) (ANTIBOD? OR IMMUNOGLOBULIN# OR HYBRIDOMA#)  
L10 89 S L9 AND PY<1992  
L11 34 DUP REM L10 (55 DUPLICATES REMOVED)  
L12 68941 S L1(S) (NEUTRALI? OR INHIBIT? OR MODULAT?)  
L13 16230 S L12(S) (ANTIBOD? OR IMMUNOGLOBULIN# OR HYBRIDOMA#)  
L14 21054 S L1(3A) (NEUTRALI? OR INHIBIT? OR MODULAT?)  
L15 5289 S L14(S) (ANTIBOD? OR IMMUNOGLOBULIN# OR HYBRIDOMA#)  
L16 906 S L15 AND PY<1992  
L17 17300 S L1(2A) (NEUTRALI? OR INHIBIT? OR MODULAT?)  
L18 4290 S L17(S) (ANTIBOD? OR IMMUNOGLOBULIN#)  
L19 685 S L18 AND PY<1992  
L20 2241 S L17(5A) (ANTIBOD? OR IMMUNOGLOBULIN#)  
L21 365 S L20 AND PY<1992  
L22 134 DUP REM L21 (231 DUPLICATES REMOVED)

=> log h

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

**WEST** Generate Collection      Print

L1: Entry 4 of 5

File: USPT

Dec 16, 1997

US-PAT-NO: 5698195

DOCUMENT-IDENTIFIER: US 5698195 A

TITLE: Methods of treating rheumatoid arthritis using chimeric anti-TNF antibodies

DATE-ISSUED: December 16, 1997

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Le; Junming	Jackson Heights	NY		
Vilcek; Jan	New York	NY		
Daddona; Peter	Menlo Park	CA		
Ghrayeb; John	Thorndale	PA		
Knight; David	Berwyn	PA		
Siegel; Scott	Westborough	MA		

US-CL-CURRENT: 424/133.1; 424/141.1, 424/142.1, 424/145.1, 514/825, 530/351, 530/387.3,  
530/388.1, 530/388.23

## CLAIMS:

What is claimed is:

1. A method of treating rheumatoid arthritis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises a non-human variable region or a TNF antigen-binding portion thereof and a human constant region.
2. The method of claim 1 wherein the non-human variable region is of murine origin.
3. The method of claim 1 wherein said anti-TNF chimeric antibody does not bind to one or more epitopes included in amino acids 11-13, 37-42, 49-57 or 155-157 of SEQ ID NO.: 1 of hTNF.
4. A method of treating rheumatoid arthritis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to monoclonal antibody cA2.
5. A method of treating rheumatoid arthritis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody binds to at least one epitope included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.:1 of hTNF.
6. A method of treating rheumatoid arthritis in a human comprising administering to the human an effective TNF-inhibiting amount of chimeric anti-TNF antibody cA2.
7. A method of treating rheumatoid arthritis, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises a non-human variable region or a TNF antigen-binding portion thereof and an IgG1 human constant region.
8. The method of claim 7 wherein the non-human variable region is of murine origin.

9. The method of claim 7 wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to monoclonal antibody cA2.

10. The method of claim 7 wherein said anti-TNF chimeric antibody does not bind to one or more epitopes included in amino acids 11-13, 37-42, 49-57 or 155-157 of SEQ ID NO.: 1 of hTNF.

11. A method of treating rheumatoid arthritis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises an IgG1 constant region and competitively inhibits binding of TNF to monoclonal antibody cA2.

12. A method of treating rheumatoid arthritis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises an IgG1 constant region and binds to at least one epitope included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.:1 of hTNF.

13. The method of claim 1 wherein the non-human variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO.: 3 and SEQ ID NO.: 5.

14. The method of claim 1 wherein the non-human variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO.: 3 and SEQ ID NO.: 5.

15. The method of claim 1 wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.: 2 and SEQ ID NO.: 4.

16. The method of claim 7 wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.: 2 and SEQ ID NO.: 4.

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L1: Entry 3 of 5

File: USPT

Jul 6, 1999

US-PAT-NO: 5919452

DOCUMENT-IDENTIFIER: US 5919452 A

TITLE: Methods of treating TNF.alpha.-mediated disease using chimeric anti-TNF antibodies

DATE-ISSUED: July 6, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Le; Junming	Jackson Heights	NY		
Vilcek; Jan	New York	NY		
Dadonna; Peter	Palo Alto	CA		
Ghrayeb; John	Thorndale	PA		
Knight; David	Berwyn	PA		
Seigal; Scott	Westborough	MA		

US-CL-CURRENT: 424/133.1; 424/145.1, 424/158.1, 530/387.3, 530/388.23, 530/389.2

## CLAIMS:

What is claimed is:

1. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to monoclonal antibody cA2.
2. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody binds to at least one epitope included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.:1 of hTNF.
3. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of chimeric anti-TNF antibody cA2.
4. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises an IgG1 constant region and competitively inhibits binding of TNF to monoclonal antibody cA2.
5. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises an IgG1 constant region and binds to at least one epitope included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.:1 of hTNF.
6. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises the non-human variable region comprising an amino acid sequence selected from

the group consisting of SEQ ID NO.:3 and SEQ ID NO.: 5.

7. A method of treating TNF.alpha.-mediated disease, other than disease resulting from infection, in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises the non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO.:3 and SEQ ID NO.: 5 and an IgG1 human constant region.

8. The method of claim 6 wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.: 2 and SEQ ID NO.: 4.

9. The method of claim 7 wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.: 2 and SEQ ID NO.: 4.

10. A method of treating TNF-.alpha.-mediated disease in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to monoclonal antibody cA2 and said disease is selected from the group consisting of immune and autoimmune pathologies, and inflammatory diseases wherein said inflammatory disease is not septic shock.

11. The method of claim 10 wherein the anti-TNF chimeric antibody is cA2.

12. A method of treating TNF-.alpha.-mediated disease in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to monoclonal antibody cA2 and said disease is selected from the group consisting of systemic lupus erythematosus, thyroidosis, graft versus host disease, scleroderma, diabetes mellitus, Graves' disease, sarcoidosis, chronic inflammatory bowel disease, ulcerative colitis, disseminated intravascular coagulation, atherosclerosis and Kawasaki's pathology.

13. The method of claim 12 wherein the anti-TNF chimeric antibody is cA2.

**WEST** Generate Collection 

L1: Entry 1 of 5

File: USPT

Sep 4, 2001

US-PAT-NO: 6284471

DOCUMENT-IDENTIFIER: US 6284471 B1

TITLE: Anti-TNF $\alpha$  antibodies and assays employing anti-TNF $\alpha$  antibodies

DATE-ISSUED: September 4, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Le; Junming	Jackson Heights	NY		
Vilcek; Jan	New York	NY		
Dadonna; Peter	Palo Alto	CA		
Ghrayeb; John	Thorndale	PA		
Knight; David	Berwyn	PA		
Siegel; Scott A.	Westborough	MA		

US-CL-CURRENT: 435/7.1; 424/133.1, 424/139.1, 424/141.1, 435/69.6, 435/70.21,  
530/387.3, 530/388.23, 530/391.3

## CLAIMS:

What is claimed is:

1. A chimeric antibody comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human tumor necrosis factor TNF. $\alpha$ ., wherein the non-human immunoglobulin variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.
2. An immunoassay method for detecting human TNF in a sample, comprising:
  - (a) contacting said sample with an antibody according to claim 1, or a TNF binding fragment thereof, in detectably labeled form; and
  - (b) detecting the binding of the antibody to said TNF.
3. A chimeric antibody comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human tumor necrosis factor TNF. $\alpha$ ., wherein the non-human immunoglobulin variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.
4. An immunoassay method for detecting human TNF in a sample, comprising:
  - (a) contacting said sample with an antibody according to claim 3, or a TNF binding fragment thereof, in detectably labeled form; and
  - (b) detecting the binding of the antibody to said TNF.
5. A chimeric antibody, comprising two light chains and two heavy chains, each of said chains comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said variable region capable of binding an epitope of human tumor necrosis factor hTNF. $\alpha$ ., wherein said light

chains comprise variable regions comprising SEQ ID NO: 3 and said heavy chains comprise variable regions comprising SEQ ID NO: 5.

6. A chimeric antibody according to claim 5, wherein the human immunoglobulin constant region is an IgG1.

7. A chimeric antibody comprising at least part of a human IgG1 constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human TNF. $\alpha$ ., wherein the non-human immunoglobulin variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.

8. A polypeptide comprising the amino acid sequence of SEQ ID NO: 3, wherein said polypeptide binds to hTNF. $\alpha$ . and competitively inhibits the binding of monoclonal antibody cA2 to hTNF. $\alpha$ ..

9. A polypeptide comprising the amino acid sequence of SEQ ID NO: 5, wherein said polypeptide binds to hTNF. $\alpha$ . and competitively inhibits the binding of monoclonal antibody cA2 to hTNF. $\alpha$ ..

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L1: Entry 1 of 3

File: PGPB

Feb 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020022720  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020022720 A1

TITLE: Anti-TNF antibodies and peptides of human tumor necrosis factor

PUBLICATION-DATE: February 21, 2002

**INVENTOR-INFORMATION:**

NAME	CITY	STATE	COUNTRY	RULE-47
Le, Junming	Jackson Heights	NY	US	
Vilcek, Jan	New York	NY	US	
Daddona, Peter	Menlo Park	CA	US	
Ghrayeb, John	Downington	PA	US	
Knight, David	Berwyn	PA	US	
Siegel, Scott	Westborough	MA	US	

US-CL-CURRENT: 536/23.1; 424/145.1

**CLAIMS:**

What is claimed is:

1. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF antibody, wherein said anti-TNF antibody competitively inhibits binding of TNF to monoclonal antibody cA2.
2. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody binds to at least one epitope included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.:1 of hTNF.
3. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of chimeric anti-TNF antibody cA2.
4. A method for treating psoriasis in a human comprising administering to the human at least one monoclonal antibody cA2, or a TNF binding fragment thereof.
5. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises an IgG1 constant region and competitively inhibits binding of TNF to monoclonal antibody cA2.
6. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti- TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises an IgG1 constant region and binds to at least one epitope included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.: 1 of hTNF.
7. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO.:3 and SEQ ID NO.:5.

8. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO.:3 and SEQ ID NO.:5 and an IgG1 human constant region.

9. The method of claim 7 wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.:2 and SEQ ID NO.:4.

10. The method of claim 8 wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO.:2 and SEQ ID NO.: 4.

11. A method of treating psoriasis in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to monoclonal antibody cA2.

12. The method of claim 1 wherein said anti-TNF antibody is a humanized antibody.

13. The method of claim 1 wherein said anti-TNF antibody is a human antibody.

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L1: Entry 5 of 5

File: USPT

Aug 12, 1997

US-PAT-NO: 5656272

DOCUMENT-IDENTIFIER: US 5656272 A

TITLE: Methods of treating TNF-.alpha.-mediated Crohn's disease using chimeric anti-TNF antibodies

DATE-ISSUED: August 12, 1997

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Le; Junming	Jackson Heights	NY		
Vilcek; Jan	New York	NY		
Dadonna; Peter	Palo Alto	CA		
Ghrayeb; John	Thorndale	PA		
Knight; David	Berwyn	PA		
Siegel; Scott A.	Westborough	MA		

US-CL-CURRENT: 424/133.1, 424/139.1, 424/145.1, 435/69.1, 435/69.6, 435/69.7,  
530/387.3, 530/388.23

## CLAIMS:

What is claimed is:

1. A method of treating TNF.alpha.-mediated Crohn's disease in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody comprises a non-human variable region or a TNF-binding portion thereof and a human constant region.
2. The method of claim 1 wherein the non-human variable region is of murine origin.
3. The method of claim 1 wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to the monoclonal antibody cA2.
4. The method of claim 1 wherein said anti-TNF chimeric antibody does not bind to one or more epitopes included in amino acids 11-13, 37-42, 49-57, or 155-157 of SEQ ID NO.: 1 of hTNF.
5. A method of treating TNF.alpha.-mediated Crohn's disease in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody competitively inhibits binding of TNF to the monoclonal antibody cA2.
6. A method of treating TNF.alpha.-mediated Crohn's disease in a human comprising administering to the human an effective TNF-inhibiting amount of an anti-TNF chimeric antibody, wherein said anti-TNF chimeric antibody binds to one or more epitopes included in amino acids between 87-108 or both 59-80 and 87-108 of SEQ ID NO.:1 of hTNF.
7. A method of treating TNF.alpha.-mediated Crohn's disease in a human comprising administering to the human an effective TNF-inhibiting amount of chimeric anti-TNF antibody cA2.